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INFORMATION DISCLOSURE STATEMENT APPLICANT

Application Number 09/893,321

Filing Dat 06/27/01

First Named Invent r Walke

Group Art Unit 1659 16 47

Examiner Name To be asigned LANDAMAN

Attorney Docket Number LEX-0195-USA

	***			U.S. PATENT DOCUMENT	rs	
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	ÃΑ	4,215,051		Schroeder et al	07/29/80	
	AB	4,376,110		David et al	03/08/83	
$\Box$	AC	4,594,595		Struckman	06/10/86	
	AD	4,631,211		Houghten	12/23/86	
	AE	4,689,405		Frank et al	08/25/87	
	AF	4,713,326		Dattagupta et al	12/15/87	
	AG	4,873,191		Wagner et al	10/10/89	
	AH	4,946,778		Ladner et al	08/07/90	
	Al	5,252,743		Barrett et al	10/12/93	
	AJ	5,424,186		Fodor et al	06/13/95	
	AK	5,445,934		Fodor et al	08/29/95	
	AL	5,459,127		Felgner et al	10/17/95	
	AM	5,556,752		Lockhart et al	09/17/96	
	AN	5,700,637		Southern	12/23/97	
	AO	5,744,305		Fodor et al	04/28/98	
	AP	5,830,721		Stemmer et al	11/03/98	
	AQ	5,837,458		Minshull et al	11/17/98	
	AR	5,869,336	一	Meyer et al.	02/09/99	
	AS	5,877,397		Lonberg et al	03/02/99	
	AT	5,948,767		Scheule et al.	09/07/99	
	AU	6,075,181		Kucherlapati et al	06/13/00	
	AV	6,110,490		Thierry	08/29/00	
$\overline{V}$	AW	6,150,584		Kucherlapati et al.	11/21/00	
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BC 1	AY	Bird et al, 1988, "Single-Chain Antigen-Binding Proteins", Science 242:423-426.	ſ
1	AZ	Bitter et al, 1987, "Expression and Secretion Vectors for Yeast", Methods in Enzymology 153:516-544.	Γ
	ВА	Colbere-Garapin et al, 1981, "A New Dominant Hybrid Selective Marker for Higher Eukaryotic Cells", J. Mol. Biol. 150:1-14.	
[	ВВ	Gautier et al, 1987, "α-DNA IV:α-anomeric and β-anomeric tetrathymidylates covalently linked to intercalating oxazolopyridocarbazole. Synthesis, physiochemical properties and poly (rA) binding", Nucleic Acids Research 15(16):6625-6641.	
E	вс	Gordon, 1989, "Transgenic Animals", International Review of Cytology, 115:171-229.	
E	BD	Greenspan et al, 1993, "Idiotypes: structure and immunogenicity", FASEB Journal 7:437-444.	ĺ
E	BE	Gu et al, 1994, "Deletion of a DNA Polymerase $\beta$ Gene Segment in T Cells Using Cell Type-Specific Gene Targeting", Science 265:103-106.	
E	BF	Huse et al, 1989, "Generation of a Large Combinatorial Library of the Immunoglobulin Repertoire in Phage Lambda", Science 246:1275-1281.	ĺ
E	BG	Huston et al, 1988, "Protein engineering of antibody binding sites: Recovery of specific activity in an anti-digoxin single-chain Fv analogue produced in Escherichia coli", Proc. Natl. Acad. Sci. USA 85:5879-5883.	ĺ
E	вн	Inoue et al, 1987, "Sequence-dependent hydrolysis of RNA using modified oligonucleotide splints and R Nase H", FEBS Letters 215(2):327-330.	Ī
E	ВІ	Inoue et al, 1987, "Synthesis and hybridization studies on two complementary nona(2'-O-methyl)ribonucleotides", Nucleic Acids Research 15(15):6131-6149.	ĺ
E	BJ	Inouye & Inouye, 1985, "Up-promoter mutations in the lpp gene of Escherichia coli", Nucleic Acids Research 13(9):3101-3110.	
E	вк	Janknecht et al, 1991, "Rapid and efficient purification of native histidine-tagged protein expressed by recombinant vaccinia virus", PNAS 88:8972-8976.	
E	BL	Kohler & Milstein, 1975, "Continuous cultures of fused cells secreting antibody of predefined specificity", Nature 256:495-497.	
E	ВМ	Lakso et al, 1992, "Targeted oncogene activation by site-specific recombination in transgenic mice", Proc. Natl. Acad. Sci. USA 89:6232-6236.	
E	BN	Lavitrano et al, 1989, "Sperm Cells ad Vectors for Introducing Froeign DNA into Eggs: Genetic Transformation of Mice", Cell 57:717-723.	
V	во	Lo, 1983, "Transformation by Iontophoretic Microinjection of DNA: Multiple Integrations without Tandem Insertions", Mol. Cell. Biology 3(10):1803-1814.	•

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BL	ВР	Logan et al, 1984, "Adenovirus tripartite leader sequence enhances translation of mRNAs late after infection", Proc. Natl. Acad. Sci. USA 81:3655-3659.	
İ	BQ	Lowy et al, 1980, "Isolation of Transforming DNA: Cloning the Hamster aprt Gene", Cell 22:817-823.	
	BR	Morrison et al, 1984, "Chimeric human antibody molecules: Mouse antigen-binding domains with human constant region domains", Proc. Natl. Acad. Sci. USA 81:6851-6855.	
	BS	Mulligan & Berg, 1981, "Selection for animal cells that express the Escherichia coli gene coding for xanthine-guanine phosphoribosyltransferase", Proc. Natl. Acad. Sci. USA 78(4):2072-2076.	
	вт	Neuberger et al, 1984, "Recombinant antibodies possessing novel effector functions", Nature 312:604-608.	
	BU	Nisonoff, 1991, "Idiotypes: Concepts and Applications", J. of Immunology 147:2429-2438.	
	BV	O'Hare et al, 1981, "Transformation of mouse fibroblasts to methotrexate resistance by a recombinant plasmid expressing a prokaryotic dihydrofolate reductase", Proc. Natl. Acad. Sci. USA 78(3):1527-1531.	
	BW	Ruther et al, 1983, "Easy identification of cDNA clones", EMBO Journal 2(10):1791-1794.	
	ВХ	Santerre et al, 1984, "Expression of prokaryotic genes for hygromycin B and G418 resistance as dominant-selection markers in mouse L cells", Gene 30:147-156.	
	BY	Sarin et al, 1988, "Inhibition of acquired immunodeficiency syndrome virus by oligodeoxynucleoside methylphosphonates", Proc. Natl. Acad. Sci. USA 85:7448-7451.	
	BZ	Smith et al, 1983, "Molecular Engineering of the Autographa californica Nuclear Polyhedrosis Virus Genome: Deletion Mutations within the Polyhedrin Gene", J. Virol. 46(2):584-593.	
	CA	Stein et al, 1988, "Physiochemical properties of phosphorothioate oligodeoxynucleotides", Nucleic Acids Research 16(8):3209-3221.	
	СВ	Szybalska & Szybalski, 1962, "Genetics of Human Cell Lines, IV. DNA-Mediated Heritable Transformation of a Biochemical Trait", Proc. Natl. Acad. Sci. USA 48:2026-2034.	
	СС	Takeda et al, 1985, "Construction of chimaeric processed immunoglobulin genes containing mouse variable and human constant region sequences", Nature 314:452-454.	
	CD	Thompson et al, 1989, "Germ Line Transmission and Expression of a Corrected HPRT Gene Produced by Gene Targetin in Embryonic Stem Cells", Cell 56:313-321.	g
	CE	Van Der Putten et al, 1985, "Efficient insertion of genes into the mouse germ line via retroviral vectors", Proc. Natl. Acad. Sci. USA 82:6148-6152.	
	CF	Van Heeke et al, 1989, "Expression of Human Asparagine Synthetase in Escherichia coli", J. Biol. Chemistry 264(10):5503-5509.	
	CG	Ward et al, 1989, "Binding activities of a repertoire of single immunoglobulin variable domains secreted from Escherichia coli", Nature 341:544-546.	
1	СН	Wigler et al, 1977, "Transfer of Purified Herpes Virus Thymidine Kinase Gene to Cultured Mouse Cells", Cell 11:223-232.	
<b>V</b>	CI	Wigler et al, 1980, "Transformation of mammalian cells with an amplifiable dominant-acting gene", Proc. Natl. Acad. Sci. USA 77(6):3567-3570.	

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BL	СК	WANG, Jia Bei et al., "The GABAA receptor gammal-subunit in seizure prone (DBA/2) and resistant (C57BL/6) mice," Brain Research Bulletin, Vol. 45, No. 4, 03/01/98, pgs. 421-425, XP002199263, ISSN: 0361-9230				
(	CL	YMER, S. et al., "Structural and Functional Characterization of the Gamma-1 Subunit of GABA-A Benzodiazepine Receptors," EMBO Journal, Vol. 9, No. 10, 1990, pgs. 3261-3267, XP002199264, ISSN: 0261-4189				
	СМ	KOFUJI, P. et al., "Generation of two forms of the gamma aminobutyric acid receptor Gamma-2 subunit in mice by alternative splicing," Journal of Neurochemistry, Vol. 56, No. 2, 1991, pgs. 713-715, XP008003427, ISSN: 0022-3042				
	CN	CHEBIB, Mary et al., "The 'ABC' of GABA receptors: A brief review," Clinical and Experimental Pharmacology and Physiology, Vol. 26, No. 11, Nov. 1999, pgs. 937-940, XP002168993				
$\downarrow$	СО	GABRYS, B., "GABA receptors," Trends in Pharmacological Sciences, Elsevier Trends Journal, Cambridge, GB, Vol. 18, No. Supplement, 1997, pgs. 42-43, XP004055261, ISSN: 0165-6147				
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